

## **REMARKS**

In the Final Action dated July 28, 2004, claims 1, 2, 6, 7, 22-25, 32-35, 42-76, 80-88 and 92-99 are pending. Claims 2, 22-55, 33, 34, 44, 52-74, 76, 80, 88, 92, 93, 97 and 99 are withdrawn from consideration as drawn to non-elected subject matter. Claims 1, 32, 75, 82-87 and 94-95 are rejected. Claims 7, 35, 81, 96 and 98 are objected to as being dependent on a rejected base claim, but would be allowable if rewritten as independent claims. Claims 42-43 and 45-51 are allowed.

This Response addresses each of the Examiner's rejections and objections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

The Examiner has required cancellation of the non-elected claims. In response, Applicants have canceled claims 2, 22-55, 33, 34, 44, 52-74, 76, 80, 88, 92, 93, 97 and 99, which are withdrawn from consideration. Applicants reserve the right to pursue the non-elected subject matter in one or more divisional applications.

Claims 1, 32, 87, and 94-95 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Reff (U.S. Patent No. 5,648,267).

According to the Examiner, Reff teaches a translationally impaired selectable marker gene by adding an ATG triplet upstream of the authentic ATG start site of the selectable marker gene. Reff allegedly teaches that the added start codon is intended to impair the translation of the selectable marker gene.

As previously submitted, the teaching of Reff is principally directed to the use of an impaired Kozak sequence to reduce the translation of a selectable marker gene. As a subsidiary feature, Reff further discloses that an out-of-frame ATG codon, placed upstream of the impaired

Kozak sequence, may further enhance the effect of the Kozak sequence impairment. However, the regulation of translation, as taught by Reff, requires a fully impaired Kozak sequence. See, col. 3, lines 25-28 and 47-50; col. 3, line 65 through line 8. Reff does not teach that the insertion of ATG codons in the 5' UTR of a gene alone, absent a fully impaired Kozak sequence, is sufficient to reduce the translation of a downstream gene.

The Examiner contends that Applicants' argument relied upon a feature that is not present in the claims. Specifically, the Examiner states that the present claims, because of the "comprising" language, do not exclude the use of a fully impaired Kozac sequence. Thus, the Examiner alleges that Reff literally meets all the limitations of the claimed invention.

In response, Applicants have added new independent claims 100-103, which substantially correspond to previous independent claims 1, 32, 75 and 87, except that the new claims define the claimed methods as introducing one or more ATG triplets, independent of any other regulatory sequence, in the 5' region of the relevant gene. In this regard, Applicants respectfully submit that the term "regulatory sequence" is well understood by those skilled in the art and includes e.g., an enhancer sequence, a CAAT sequence or a capping sequence, as described in the specification, e.g., at page 41, lines 5-13. The specification clearly discloses that modification of the expression of a gene can be achieved by introducing one or more ATG triplets in the 5' UTR region of a relevant gene, absent other genetic modifications to the 5' UTR of the gene – that is, independent of any other regulatory sequence. See, e.g., page 20, lines 11-17; page 25, lines 8-16; page 30, lines 16-18; page 34, lines 4-7; pages 60-61. No new matter is introduced by claims 100-103.

Applicants respectfully submit that Reff does not teach the methods, as presently recited in claims 100-103.

Furthermore, with respect to claims 1, 32, and 75, Applicants have amended these claims to incorporate the delineation of allowable dependent claims. Specifically, claims 1, 32 and 75 have been amended to incorporate the delineations relating to termination signals of claims 7, 35 and 81, respectively, which the Examiner has indicated as allowable. Claims 7, 35 and 81 are therefore canceled. Similarly, Applicants have amended independent claim 87 to also incorporate a delineation relating to introducing a termination signal. Applicants reserve the right to pursue the subject matter embodied in the claims as originally filed in a continuation application. Applicants respectfully submit that as amended, claims 1, 32 and 75 are patentably distinct from Reff.

Applicants further respectfully submit that claims 82-86 presently depend from claims 75 and 102; claims 94-95 presently depend from claims 87 and 103. It is respectfully submitted that dependent claims 82-86 and 94-95 are also patentably distinct from Reff.

In view of the foregoing, it is respectfully submitted that the presently claimed methods are not taught by Reff. Withdrawal of the rejection under §102(b) based on Reff is therefore respectfully requested.

Claims 1, 32, 75, 87, and 94-95 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Reff in view of Haselkorn et al. (U.S. Patent No. 6,306,636 B1).

Moreover, Claims 1, 32, 75, 82-87, and 94-95 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Reff and Haselkorn et al., and further in view of Engler et al. (U.S. Patent No. 5,262,316) and Hansen et al. (U.S. Patent No. 6,051,409).

Applicants respectfully submit that Reff does not teach or suggest the claimed methods as presently recited. Applicants further submit that none of the secondary references cure the deficiencies of Reff. Therefore, the claimed methods are not obvious over Reff in

combination with any one of the secondary references. Withdrawal of the rejections under 35 U.S.C. §103(a) is therefore respectfully requested.

The Examiner has indicated that claims 96 and 98 would be allowable if rewritten in independent form to include all the limitations of the base claim and any intervening claims. Applicants have rewritten claims 96 and 98 to include the delineations of previous claim 1 and claim 32, respectively.

In view of the foregoing amendments and remarks, the present application is in condition for allowance which action is earnestly solicited.

Respectfully submitted,



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